Mexidol®

International Non-Proprietary Name (INN): Mexidol (Emoxypine)

Dosage Form: 50 mg/mL, solution for intravenous and intramuscular administration

Structure:
Active ingredient: ethylmethylhydroxypyridine succinate.
1 mL of the solution contains 50 mg of ethylmethylhydroxypyridine succinate.
2 mL ampoule contains 100 mg of ethylmethylhydroxypyridine succinate.
5 mL ampoule contains 250 mg of ethylmethylhydroxypyridine succinate.
Excipients: sodium metabisulfite – 0.4 mg in 1 mL of the substance, water for injection.

Description: Transparent colorless or slightly yellowish liquid.

Pharmacological group: antioxidant

ATC code: N07XX

Pharmacological action:

The substance has antihypoxic, membrane-protective, nootropic, anticonvulsant, anxiolytic effect, increases the body's resistance to stress. The drug increases the body's resistance to the effects of major damaging factors, to oxygen-dependent pathological conditions (shock, hypoxia and ischemia, impaired cerebral circulation, intoxication with alcohol and antipsychotic drugs (neuroleptics)). Stabilizes membrane structures of blood cells (erythrocytes and platelets) in hemolysis.

Mexidol improves cerebral metabolism and blood supply to the brain, improves microcirculation and rheological properties of blood, reduces platelet aggregation. It has a hypolipidemic effect, reduces the level of total cholesterol and low-density lipoprotein (LDL).

Mexidol normalizes metabolic processes in ischemic myocardium, reduces the zone of necrosis, restores and improves the electrical activity and contractility of myocardium, and increases coronary blood flow in the zone of ischemia, reduces the effects of reperfusion syndrome in acute coronary insufficiency. Increases the antianginal activity of nitropreparations.

Mexidol promotes preservation of retinal ganglion cells and optic nerve fibers in progressive neuropathy, the causes of which are chronic ischemia and hypoxia. Improves the functional activity of the retina and optic nerve, increasing visual acuity.

Reduces enzymatic toxemia and endogenous intoxication in acute pancreatitis.

Pharmacodynamics:
The mechanism of action of the drug Mexidol is due to its antihypoxant, antioxidant and membrane-protective action. It inhibits lipid peroxidation processes, increases superoxide dismutase activity, increases lipid-protein ratio, decreases membrane viscosity, increases membrane fluidity. Modulates the activity of membrane-bound enzymes (calcium-independent phosphodiesterase, adenylate cyclase, acetylcholinesterase), receptor complexes (benzodiazepine, gamma-aminobutyric acid (GABA), acetylcholine), which enhances their ability to bind to ligands, helps to preserve the structural and functional organization of biomembranes, transport of neurotransmitters and improve synaptic transmission. Mexidol increases the content of dopamine in the brain. It enhances compensatory activity of aerobic glycolysis and decreases the degree of inhibition of oxidative processes in the Krebs cycle under hypoxia with an increase in adenosine triphosphate (ATP), creatine phosphate and activation of energy-synthesizing functions of mitochondria, stabilization of cell membranes.

Pharmacokinetics:
Absorption: When administered intramuscularly, it is detected in blood plasma within 4 h after administration. Time to reach

maximum concentration Tmax is 0.45-0.5 h. Cmax at a dose of 400-500 mg is 3.5-4.0 μg/mL.
Distribution: Rapidly passes from the bloodstream to organs and tissues and is rapidly eliminated from the body. The time of retention of the drug (MRT) is 0.7-1.3 h.
Biotransformation: Metabolized in the liver by glucuron conjugation. Five metabolites have been identified: 3-oxypyridine phosphate - formed in the liver, breaks down into phosphoric acid and 3-oxypyridine with the participation of alkaline phosphatase; the 2nd metabolite is pharmacologically active, formed in large amounts and detected in the urine on 1-2 days after administration; the 3rd metabolite is excreted in large amounts with urine; the 4th and 5th metabolites are glucuronconjugates.
Elimination: The drug is excreted mainly with urine, mainly in the glucuronconjugated form and in minor amounts in unchanged form.

Intended uses:

- acute disorders of cerebral circulation;
- traumatic brain injury, consequences of traumatic brain injury;
- dyscirculatory encephalopathy;
- chronic cerebral ischemia;
- vegetative dystonia syndrome;
- mild (moderate) cognitive disorders;
- anxiety disorders in neurotic and neurosis-like states;
- acute myocardial infarction (from the first day) as part of complex therapy;
- primary open-angle glaucoma of various stages, as part of complex therapy;
- withdrawal syndrome in alcoholism with predominance of neurosis-like and vegetative-vascular disorders;
- acute intoxication with antipsychotic drugs;
- acute purulent-inflammatory processes of the abdominal cavity (acute necrotizing pancreatitis, peritonitis) as part of complex therapy.

Contraindications:

Individual intolerance to the drug components, acute renal failure and acute hepatic failure. It is not recommended for children, pregnant and lactatingwomen due to the lack of clinical research data.

Dosage and administration:

Adults: the maximum daily dose should not exceed 1200 mg.
Intramuscularly or intravenously (stream or drip). Stream infusion of Mexidol is administered slowly for 5-7 minutes, drip - at a rate of 40-60 drops per minute.

- In acute cerebral circulation disorders Mexidol is used during the first 10-14 days intravenously (IV) by drip 200-500 mg 2-4 times a day, then intramuscularly (IM) 200-250 mg 2-3 times a day for 2 weeks, after that it is recommended to switch to oral dosage forms.
- In traumatic brain injury and its consequences Mexidol is used for 10-15 days by IV drip 200-500 mg 2-4 times a day, after which it is recommended to switch to oral dosage forms.
- In dyscirculatory encephalopathy in the decompensation phase, Mexidol should be administered by stream infusion or by drip at a dose of 200-500 mg 1-2 times a day for 14 days. Then it should be administered IM at 100-250 mg per day for the next 2 weeks, after which it is recommended to switch to oral dosage forms.
- For course prevention of dyscirculatory encephalopathy the drug is administered IM in a dose of 200-250 mg 2 times a day for 10-14 days, after which it is recommended to switch to oral dosage forms.
- In chronic cerebral ischemia Mexidol should be administered in 10 ml (500 mg) once a day by IV drip or IV stream slowly for 14 days, after which it is recommended to switch to oral dosage forms.
- In mild (moderate) cognitive disorders Mexidol should be administered in 10 ml (500 mg) once a day by IV drip or IV stream slowly for 14 days, after which it is recommended to switch to oral dosage forms.
- In anxiety disorders the drug is used intravenously in a daily dose of 100-300 mg per day for 14-30 days, after which it is recommended to switch to oral dosage forms.

- In acute myocardial infarction as part of complex therapy Mexidol is administered IV or IM for 14 days against the background of conventional therapy of myocardial infarction, including nitrates, beta-adrenoblockers, angiotensin-converting enzyme (ACE) inhibitors, thrombolytics, anticoagulant and antiaggregant agents, as well as symptomatic agents as indicated. To achieve the maximum effect, within the first 5 days, the drug should be administered IV, in the next 9 days - IM. IV administration is performed by drip infusion, slowly (to avoid side effects) with 0.9% sodium chloride solution or 5% dextrose (glucose) solution in the volume of 100-150 ml for 30-90 minutes. If necessary, slow stream infusion for at least 5 minutes is possible. Administration of the drug (IV or IM) is performed 3 times a day every 8 hours. The daily therapeutic dose is 6-9 mg/kg body weight per day, single dose - 2-3 mg/kg body weight. The maximum daily dose should not exceed 800 mg, single dose - 250 mg.
- In open-angle glaucoma of various stages as a part of complex therapy Mexidol is administered by IM 100-300 mg per day, 1-3 times a day for 14 days.
- In withdrawal alcohol syndrome Mexidol is administered in a dose of 200-500 mg IV drip or IM 2-3 times a day for 5-7 days.
- In acute intoxication with antipsychotic agents, the drug is administered intravenously at a dose of 200-500 mg per day for 7-14 days.
- In acute purulent-inflammatory processes of the abdominal cavity (acute necrotizing pancreatitis, peritonitis) the drug is administered in the first day of both preoperative and postoperative periods. The administered doses depend on the form and severity of the disease, the spread of the process, variants of the clinical course. The drug should be canceled gradually only after a stable positive clinical and laboratory effect.
- In acute edema (interstitial) pancreatitis Mexidol is administered 200-500 mg 3 times a day, IV drip (in 0.9% sodium chloride solution) and IM. Mild severity of necrotizing pancreatitis - 100-200 mg 3 times a day IV drip (in 0.9% sodium chloride solution) and IM. Medium severity - 200 mg 3 times a day, IV drip (in 0.9% sodium chloride solution). Severe course - in pulse dosage of 800 mg on the first day, with two-time mode of administration; further on 200-500 mg 2 times a day with a gradual decrease in the daily dose. Extremely severe course - in the initial dosage of 800 mg per day until persistent relief of manifestations of pancreatogenic shock, after stabilization of the condition 300-500 mg 2 times a day by IV drip (in 0.9% sodium chloride solution) with a gradual decrease in daily dosage.

How to make Mexidol IM injection:

1) Wash your hands thoroughly with soap and water and prepare the following items: medication prescribed by your doctor, a disposable syringe with a needle, alcohol wipes or alcohol solution with cotton pads.
2) Choose the area to be injected. The most suitable injection site is upper outer square of the buttock or thigh.
3) Open the ampoule and fill the syringe with the solution. Holding the syringe with the needle up, tap it with a finger to allow air bubbles to accumulate in the upper part, then remove the air by pressing the syringe plunger until drops of solution appear.
4) Wipe the selected injection site an alcohol pad.
5) Stretch the skin at the site of the injection. Introduce 2/3 of the needle at the angle of 90° (i.e., perpendicular) with a sharp and confident movement. Slowly press on the piston to inject the drug. After manipulation, it is necessary to clamp the puncture site with an alcohol wipe and massage a little.

In case of unpleasant symptoms that do not go away within a few minutes and may threaten your health/life, an ambulance should be called immediately!

Side effects:

- Immune system disorders: very rare - anaphylactic shock, angioedema, urticaria.
- Mental disorders: very rare - drowsiness.
- Nervous system disorders: very rare - headache, dizziness (may be associated with an excessively fast rate of

administration and is short-term).

- Vascular disorders: very rare - decreased blood pressure (BP), increased BP (may be associated with an excessively high rate of administration and is short-term).
- Respiratory system, chest and mediastinal organs disorders: very rare - dry cough, throat congestion, chest discomfort, difficulty breathing (may be associated with excessively high rate of administration and is of short-term nature).
- Gastrointestinal disorders: very rare - dry mouth, nausea, unpleasant odor, metallic taste in the mouth.
- Skin and subcutaneous tissue disorders: very rare - itching, rash, hyperemia.
- General disorders and reactions at the injection site: very rare - sensation of warmth.

To avoid adverse reactions, it is recommended to follow the dosing regimen and the rate of drug administration.

Overdose:
Drowsiness, insomnia. Due to low toxicity, overdose is unlikely. Treatment is usually not required; symptoms tend to disappear within 24h. In case of severe reactions, supportive and symptomatic treatment is carried out.

Interaction with other drugs:
This medicinal product should not be mixed with other compounds, except for those used for preparation of solution for infusion (0.9% sodium chloride solution or 5% dextrose (glucose) solution). Mexidol enhances the action of benzodiazepine anxiolytics, anticonvulsants (carbamazepine) and antiparkinsonian medicines (levodopa). Mexidol reduces the toxic effect of ethanol.

Special instructions:
In some cases, especially in predisposed patients with bronchial asthma and increased sensitivity to sulfites, severe hypersensitivity reactions and bronchospasm can occur.

Pregnancy and lactation:
Mexidol is not recommended during pregnancy and lactation.

Influence on the ability to drive vehicles and operate mechanisms:
During the treatment period, care must be taken when driving vehicles and engaging in other potentially hazardous activities that require increased concentration of attention and speed of psychomotor reactions.

Storage conditions: store in a dry dark place at temperatures no higher than 25°C (77°F). Keep out of reach of children.

Shelf life: 3 years. Do not use beyond the expiration date printed on the package.

Manufacturer: Pharmasoft, Russia. https://pharmasoft